BODY'S BATTLES

BAL PHONDKE
Foreword

The Council of Scientific & Industrial Research (CSIR), established in 1942, is committed to the advancement of scientific knowledge, and economic and industrial development of the country. Over the years CSIR has created a base for scientific capability and excellence spanning a wide spectrum of areas enabling it to carry out research and development as well as provide national standards, testing and certification facilities. It has also been training researchers, popularizing science and helping in the inculcation of scientific temper in the country.

The CSIR today is a well knit and action oriented network of 41 laboratories spread throughout the country with activities ranging from molecular biology to mining, medicinal plants to mechanical engineering, mathematical modelling to metrology, chemicals to coal and so on.

While discharging its mandate, CSIR has not lost sight of the necessity to remain at the cutting edge of science in order to be in a position to acquire and generate expertise in frontier areas of technology. CSIR's contributions to high-tech and emerging areas of science and technology are recognised among others for precocious flowering of tissue cultured bamboo, DNA finger printing, development of non-noble metal zeolite catalysts, mining of polymetallic nodules from the Indian Ocean bed, building an all-composite light research aircraft, high temperature superconductivity, to mention only a few.

Being acutely aware that the pace of scientific and technological development cannot be maintained without a steady influx of bright young scientists, CSIR has undertaken a vigorous programme of human resource development which includes, inter alia, collaborative efforts with the University Grants Commission aimed at nurturing the budding careers of fresh science and technology graduates.

However, all these would not yield the desired results in the absence of an atmosphere appreciative of advances in science
and technology. If the people at large remain in awe of science and consider it as something which is far removed from their realms, scientific culture cannot take root. CSIR has been alive to this problem and has been active in taking science to the people, particularly through the print medium. It has an active programme aimed at popularization of science, its concepts, achievements and utility, by bringing it to the doorsteps of the masses through both print and electronic media. This is expected to serve a dual purpose. First, it would create awareness and interest among the intelligent layman and, secondly, it would help youngsters at the point of choosing an academic career in getting a broad-based knowledge about science in general and its frontier areas in particular. Such familiarity would not only kindle in them deep and abiding interest in matters scientific but would also be instrumental in helping them to choose the scientific or technological education that is best suited to them according to their own interests and aptitudes. There would be no groping in the dark for them. However, this is one field where enough is never enough.

This was the driving consideration when it was decided to bring out in this 50th anniversary year of CSIR a series of profusely illustrated and specially written popular monographs on a judicious mix of scientific and technological subjects varying from the outer space to the inner space. Some of the important subjects covered are astronomy, meteorology, oceanography, new materials, immunology and biotechnology.

It is hoped that this series of monographs would be able to whet the varied appetites of a wide cross-section of the target readership and spur them on to gathering further knowledge on the subjects of their choice and liking. An exciting sojourn through the wonderland of science, we hope, awaits the reader. We can only wish him Bon voyage and say, happy hunting.
Preface

"War makes rattling good history" so said Oscar Wilde. He was of course referring to the macroscopic struggles engaged in by nations to capture new territories or to merely retain old ones. These conflicts are highly visible and now, with ready help from the electronic media, brought to one's family room. But some other battles not visible to the naked eye, even with technological aids, are equally fascinating. A vivid account of these miniscule wars fought within the confines of the human body would be equally breathtaking if only for the fact that these are quite literally "life and death" struggles. And they are fought every single living moment. The body's sentinels cannot afford to lower their guard even for the brief moment it takes to bat an eyelid, such is the cunning, guile and multitude of the microbial enemies. It would be unfair though to crib about man having been placed in such a hostile environment all alone and without a shield. For nature has endowed the human body with a built-in defence organization that can be the envy of the most modern technologically advanced nation. The intricate network of checks and balances to keep the armed forces fighting fit at all times, the diversity of the armament, resulting in weapons tailor-made to defeat the enemy, and the sophistry of strategy making it possible to meet squarely every imaginable threat make the defence of the human body a unique operation. Having learnt about this most valuable gift of nature man has used his knowledge to strengthen the defence and hone its combatworthiness even further. That is why, notwithstanding the occasional snafu, the body emerges victorious in its battle most of the time.
Acknowledgements

The grand design for “Body’s Battles” was drawn over a number of years. The trigger to put it into action was provided by the proposal to launch the popular science series in celebration of the Golden Jubilee of the CSIR. “Body’s Battles” was identified as the first salvo to be fired in this campaign. The detailed battle-plans were then prepared and were put on paper by Abdul Rauf and Shammi Gupta. Drafts of these in various states of preparation were seen by friends like Raju Bhisey, S.S. Saksena, Ramesh Kamat, Saibal Kumar Nag and D. Balasubramanian whose criticism, at times harsh but always constructive, have helped hone them further. But the final razor-edge sharpness was acquired only after they survived the vigilant eye and red pencil of the volume editor, Sukanya Datta.

Additional ammunition in the form of visual displays was eagerly, and expertly, provided by Pradip Banerjee and Neeru Sharma. Marching orders were issued after due copy editing, proof reading and other detailed check up by Radhe Shiam. The credit for putting everything in the final trim shape goes to K.B. Nagpal and Sudhir Chandra Mamgain under the overall command of K. Satyanarayana and V. Ramachandran. If “Body’s Battles” scores a success, a major share would be due to these loyal troops and commanders.

Bal Phondke
To

DR. KRISHNA SAINIS

in remembrance of
successful "immunological collaboration"

and to

his equally talented better half

DR. JAYASHREE SAINIS

— Bal
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The enemy enters, its advance guard taking one step at a time. Stealth and deceit are its bywords. Emboldened by the apparent absence of any challenge or hurdles, it beckons some of its followers to forge ahead. It aims at establishing a firm base from where further inroads could be made into the alien territory.

The defence forces, however, have not slackened their vigil. They have noticed the appearance of the trespasser. Unbeknownst to him they have even examined his passport, thereby establishing his identity. They have made sure that the gatecrasher is no friend; nor is he an innocent wanderer.

Having thus sensed his inimical intent, they have alerted the command headquarters which readily gets into action. It calls for a general mobilization in an attempt to increase the number of soldiers. Simultaneously, it issues a battle order to all the garrisons located at strategic points all over the territory.

Heeding the call for action, the entire defence set-up rises to the occasion. Even as some of the troops, particularly the suicide brigades, start donning the ar-
The body is a well defended fortress.
mour and limbering up the tanks, the ammunition factories put their assembly lines into top gear. The guided missiles manufactured by the latter are tailor-made to meet the enemy threat. Once fired, they go chasing the enemy ranks like homing hawks. And on encountering the foe face-to-face, they embrace him in an Indian death lock, choking life out of him. The battle is on.

The battlefield is now strewn with corpses, mostly those of the enemy troops, though there are a few belonging to those loyal fighters who have laid down their lives in the line of duty. The scavenger units which were standing by in readiness, never in doubt of the ultimate victory, now commence their show. Swiftly, they clear the debris and throw out the rubble. All that remains now is to repair the damage and restore the damaged assets.

This is not the scenario of an imaginary war. Such wars are waged every single living moment giving credence to what the Marathi saint-poet Tukaram had declared in one of his famous Abhangas, “Ratran Din Amha Yuddhacha Prasanga” (Every single living moment we are in a state of war). If these wars are not easily discernible it is because the enemy, the defending armies, the arsenal as well as the battlegrounds are all microscopic in nature. The wars are all fought within the human body.

Man is the most evolved animal and thus could be considered as the fittest living being nature has produced. Putting to use the faculty of intelligence that nature has endowed him with, man has further shored his defences by amassing an impressive range of weaponry. Yet, sadly, all this ammunition fails when it comes to defending his own body against the multitude of invisible, microscopic, disease-bearing organisms that surround him. So much so that a scientist had been moved to state that man is floating in an ocean of microbes.
"Man is floating in an ocean of microbes"
It will not be fair, however, to crib about nature being unkind to us. Because the number and range of the miniscule adversaries are so large, it may appear that the human species is let loose among a vast crowd of these tiny foes much like babes in deep, dark, frightening woods. But nature herself has gifted the human body with a built-in defence system that can be the envy of the most militarily advanced nation today. The defence organization of the human body is so efficient, so well structured and so combatworthy that it can very well adopt for itself the now familiar slogan “neighbour’s envy, owner’s pride”.

A soldier is the basic constituent of an army. An alert army has a programme for continuous recruitment. The raw recruit has, however, to be made physically fit, given a general sense of discipline, taught to distinguish friend from foe, made to learn the principles and use of modern weaponry and trained for combat. Modern armed forces are diversified. They consist not only of the three wings that fight wars on land, sea and in air but even of the more specialized contingents like artillery, signal corps, corps of engineers, or the sea-air wing, paratroopers and commandos. Depending upon his final deployment, the graduate trainee has to be given advanced training in one of the specialized tasks.

Trained and equipped, the soldier cannot be left on his own to become a lonely warrior. For effective defence the jawans have to be grouped into platoons, companies, battalions and brigades of optimum sizes. Garrison units have to be located at strategic points. And constant vigil has to be maintained at all the borders and potential entry points of the enemy. The activities and battleworthiness of all these units have to be overseen by the central command which also instructs all the distant units regarding their duties from time to time.

Such would be the structure of any well organized efficient army. The body’s defence system possesses all these attributes and some more.
The sentinel that constitutes this corporeal army are the lymphocytes which are a type of white blood cells. When fully trained and ready to go into active service they are armed with a singular ability that permits them to distinguish between self and non-self. This enables them to sift the grain from the chaff or food from poison; in other words, friend from foe. The distinguished Australian Nobel laureate Sir Frank MacFarlane Burnet (1899 - 1985) first deciphered the mysterious ways in which these body-soldiers were able to find out if the new entrant was
an ally or had come with dishonourable intentions. He enunciated the principle of self and non-self which guides the working of the body's jawans.

Sir Frank MacFarlane Burnet enunciated the concept of SELF and NON-SELF prominently on its surface. The tag comes in the form of a molecular configuration that belongs only to that particular entity and to none else. In scientific jargon this standard bearer of a substance is called the antigen.

Another type of cells, macrophages which literally means giant-sized eaters, assist the lymphocytes in the identification parade. They engulf the incoming substance and present only its identity card on their surface conveniently adjacent to
The recruiting centre for the body's jawans is the bone marrow, the porridge-like substance that resides in the hollow interior of the bones. This is the progenitor of all types of blood cells. The mother cell of all the leucocytes, the white blood cells, is the pluripotent stem cell in the bone marrow. As its name suggests, it has the potential to develop along more than one track. Some of these become the lymphoid stem cells. Others proceed to turn into myeloid stem cells which go on to develop into a vast array of cells like mast cells, polymorphonuclear granulocytes and macrophages. These cells also play an...
effective role in the body's defence, though the central role is reserved for the lymphocytes.

By the time the lymphocytes leave the bone marrow they are put through all the paces that make them a soldier. The generalized training equips them with the attributes that make them a useful member of the defence network.

However, for modern warfare a general training that instills discipline, physical fitness and familiarity with light combat is not enough. A modern military comprises various specialized units, each entrusted with a specific task, for which it is suitably equipped. Accordingly, some units specialize in armoured warfare, some in communication, yet another in handling long range missiles.

The body's armed forces are no exception. They too are organized into at least two major, and a host of minor, specialized constituents. There are two centres of advanced training for the lymphocytes that have matured in the bone marrow. In the birds one of these is the organ known as the Bursa of Fabricius. In mammals this organ is absent. Yet, in these animals and in humans too, a functional equivalent of the Bursa exists. Though there is no unanimity about its precise identity, the predominant view among scientists today is that it is the bone marrow itself. Those cells which acquire advanced training in this centre become the B-lymphocytes.

The other school of advanced training is the thymus which is a white bi-lobed organ sitting astride the heart. It is fairly big at birth but slowly gets reduced in size as one attains adulthood. Cells that have a sojourn through the thymus develop into the T-lymphocytes.

The functional activities of these two wings are distinctly different. Particularly in the molecular receptors on their surface the two cell types differ markedly. For example, the human T-cells have the fortuitous property of binding sheep red blood cells (SRBC). If human lymphocytes are mixed with
SRBC and incubated, the SRBC cluster around T-cells forming rosettes. This was one of the first structural differences discerned among the two cells. Today, however, a battery of more sophisticated molecular surface markers of identity are available to the scientists.

There is a third population of lymphocytes that show the attributes of neither the T- nor the B-cells. All three cell types show certain common features that qualify them to be classified as lymphocytes. But each of them possesses individual markers in addition. It is like a paratrooper sporting an additional badge besides the crossed swords of the army or the wings of the air force.

The average human adult has about $10^{11}$ (100 billion) lymphoid cells. That makes up roughly two per cent of the total body weight. The lymphocytes constitute one-fifth of the total white blood cells. The proportion of the specialized component units varies. But on an average 5-15 per cent of all the lymphocytes are B-cells, 65 to 75 per cent are the T-cells and the remaining 20 per cent is made up by the third population.
Basically, the T-cells constitute a much diversified force, while the B-cells remain content at playing a secondary, though, an equally crucial role. The T-cells not only collaborate with the macrophages in examining the credentials of every entrant, whether native or foreign, but also get activated the moment the stranger’s malafide intentions become clear.

A group of such activated T-cells goes around in search of those B-cells that are armed with the blueprint for a magic bullet that will cook the goose of the enemy in a highly specific manner. These T-cells approach such B-cells and actively help them in the manufacture of those specific guided missiles called the antibodies. These are called the helper T-cells (T_H).

There is a second type of T-cells that girds its loins for a harakiri type of attack on the entrenched enemy by strapping deadly weapons to its body and crashlanding on the enemy. These are called the cytotoxic or killer T-cells (T_C).

There is yet another type of T-cells that ensures that neither the helpers nor the killers get overenthusiastic. They maintain a sense of proportion so that the war-effort is kept at the optimum level. They do not hesitate to crackdown on their own ilk should the latter show tendencies of running amok. These are known as the suppressor T-cells (T_s).

Usually a finely tuned balance is maintained between the strengths of the helper and suppressor forces. The whole machinery then remains fighting fit and the body trim. If either of the arms become dominant upsetting the delicate balance it can be ruinous. This is best exemplified by the much dreaded AIDS, the virus responsible for which attacks the helper force and renders it hors de combat. The suppressor units thus get an upper hand. Being loyal and highly disciplined troops they continue to restrict the immune response thus unwittingly aiding the enemy rather than the host body.
Though the third population of non-T, non-B cells does not display any tell-tale structural markers it possesses a distinct functional attribute. These cells possess the ability to kill certain tumour cells. The TH- cells help the B-cells to make the antibody missiles. The TC-cells on the other hand are capable killers on their own.
cells, cells infected by a virus which have been coated with or target cells antibodies.

They are, therefore, referred to as **natural killer** cells (NK) different from the killer T-cells which acquire the licence to kill only after the encounter with an enemy. Further, that
The finely tuned attack system acts in concert as soon as a NON-SELF invasion is recognized.
licence extends specifically to that enemy and none else whereas the NK cells lack this specificity.

These highly trained troops are obviously organized into garrisons of optimum size and located at strategic positions. These garrisons are known as lymph nodes. The body's enemies, the pathogenic bacteria, viruses, fungi, can try to gain entry with the air we breathe. To check them there are paratracheal lymph nodes studded along the windpipe. Food and water can provide another source of entry. The mesenteric lymph nodes lining the gut from outside confront these. Some enterprising pathogens might try to pierce the skin and enter. They will have to contend with a network of lymph nodes just under the skin all along the body.

In addition there is a major command centre in the spleen, the red sausage-shaped organ located under the stomach on the left side. The spleen is a major lymphoid organ and plays a crucial role in the active battle against the enemy microbe. The tonsils as well as Peyer’s Patches on the outside of the small intestine constitute other such units.

Besides these batallions posted at specific sites there is a roving patrol of lymphocytes that constantly traverses the entire territory by travelling with the blood stream. In fact, even the troops from various garrison units also travel from time to time to the blood and back. The lymphocyte soldiers keep a close vigil all the time.
Howsoever well equipped and trained an army may be, unless there are basic fortifications preventing the enemy from merrily walking in, the territory cannot be easily defended. Nature knows this only too well and has endowed the body with such front line defences. Only when the enemy succeeds in breaching these barriers do the troops start engaging the enemy ranks in combat.

The foremost among these barriers is the skin. Being waterproof it remains impenetrable to most invaders. Further it produces certain fatty acids which are toxic to many a microorganism.

Of course, there are certain areas of the body that are not covered by the skin; for example eyes, mouth and internal ears. Likewise, lungs and intestinal tract are also open and accessible to marauding microbes. Keeping this in mind, nature has made provision of alternative defences for these organs. Tears, saliva or such other bodily secretions which bathe some of these organs contain a special substance, an enzyme called lysozyme. This can split molecules that form constituent units of the outer envelope of some bacteria. This
leads to the killing of those microbes.

There are other ways nature has devised to

- Tears in the eye
- Hair in the nose
- Cilia in the airways
- Sebaceous secretions of the skin
- Acid in the stomach
- Friendly bacteria in the vagina as also in the gut

The body has inbuilt barriers to invasion by harmful microbes: tear drops contain lysozyme that can kill bacteria.
tackle the trespassers. Mucus in the nose and airways, for example, can engulf the bacteria, immobilizing them. This also prevents them from penetrating deeper into the tissue. The tiny hair-like structures in the nasal passage, the cilia, then brush this mucus-ball into the throat from where through the swallowing action it passes to the stomach. The acid which is constantly secreted in the stomach to help in digestion kills most of the microorganisms that have wittingly or unwittingly reached there.

Nature also follows the adage, 'it takes a thief to catch a thief'. As a consequence a number of bacteria that are normal residents of our guts and which play a crucial role in digestion also pitch in by occupying all the nooks and corners of the innards, thereby denying the intruders even a toehold. Similar friendly microbes live on the skin and in the vagina. In the latter, they eat up carbohydrates to produce lactic acid. The environs are thus made hostile to many bacteria, viruses and fungi.

Most often than not the intruder will be dissuaded from encroaching further. Better still it will be thrown out of the territory altogether. Should an enemy agent succeed in hoodwinking this vigilant border security force it will have to contend with the invincible defence system or to use the scientists' language, the immune system.

The response of the defence organization to any invasion is called the immune response. This involves identification of the entrant, alerting the various command centres, engaging the enemy in a battle royal, clearing the debris as well as repairing and reconstructing of the damage done to the tissues.

Like any modern fighting force the body's army does not depend on a single strategy or a solitary weapon. It has devised at least two major types of offensives, the cellular immune response and the humoral immune response.
The former resembles a blitzkrieg involving assault by the tank brigade. In this, the killer Tc-cells themselves march up to the enemy ranks and kill them. The distinguishing feature of the humoral response, on the other hand, is the manufacture of a highly specific, almost tailor-made guided missile, the antibody molecule. This is produced by a type of B-cells following a collaborative endeavour with the Th-cells. It is then launched into the bloodstream and goes in search of the enemy, ultimately destroying it. Of course, variations of these strategies that suit the exigencies best, are usually employed.

The armoured brigade of Tc-lymphocytes and/or the missile attack by antibodies usually always triumph over the microbial invaders.
The antigen-antibody reaction is highly specific because the antibodies are tailor made for the antigen.

Whichever offensive may be ultimately chosen the preparations follow a tried and tested path. As soon as an alien organism enters, it is surrounded by the macrophages or certain other cells whose job is to scan the antigenic passport of the intruder. These police cells then display this antigenic identity tag to the helper T-cells. Simultaneously,
they show to the T\textsubscript{H} cells their own identity card in the form of a protein molecule called the MHC protein. This enables the T\textsubscript{H}-cells not only to satisfy themselves that the presenting police cell is a genuine sentry and not a masquerading spy but also to compare the two cards to make sure that the intruder is indeed a trespasser. This mechanism also guarantees that enthusiastic T\textsubscript{H}-cells do not start a war, even by mistake, against its own kind.

The moment a foreign enemy agent is thus recognized, the T\textsubscript{H}-cell also receives a chemical messenger from the sentry cell. This induces the T\textsubscript{H}-cell to divide and increase its ranks. These mobilized T\textsubscript{H}-cells then go on looking for the appropriate armament-producing factories, the B-cells.

There pre-exist a large diversity of these factories, each capable of producing the right type of missile tailor-made for the particular enemy. The precise identification of the right factory by the T\textsubscript{H}-cell takes place in the same manner in which the enemy agent is recognized.

The T\textsubscript{H}-cell immediately gives the armament production plant the green signal, again in the form of a chemical message. This goads these cellular factories, first to duplicate themselves to create an army of these manufacturing units, each of which then undertakes the production of a highly specific antibody.
Antibodies are protein molecules of a globular nature. Like all proteins they are made up of long chains of **amino acids**, somewhat like strings of beads of different sizes or shapes. There are two pairs of such chains in every molecule. One pair of chains, both members of which are totally identical, is about twice as long as the other pair. Therefore, the smaller of these are called light chains. These consist of approximately 220 amino acids each. The bigger chains are called the heavy chains, each of which is made up by linking 450 amino acids. Each light chain is linked to a heavy chain by a bridge between two sulphur atoms. The two heavy chains are likewise coupled together with a **disulphide bridge**. The entire antibody molecule looks like the capital letter Y or rather like a slingshot. The places where a piece of elastic is attached to the sling are the active centres. It is with these arms that the antibody missile latches on to the antigen firmly.

Both the chains take part in this antigenic capture. Scientists have likened this to holding an apple with fingers of both hands. Since the hinge region of the Y-shaped molecule is flexible, the antibody arms can bend when necessary. The molecule then looks like a capital T.

The exact sequence of the amino acids in a chain gives it its own special character. Since there are such large numbers of these in each chain, every antibody molecule already acquires a character different from others in many ways. A closer look at the anatomy of these molecules, however, makes it clear how each antibody becomes unique.

Two scientists in particular, Rodney **PORTER** (1917-1985) and Gerald **EDELMAN** (1929- ), discovered the secrets of the structure of an antibody missile. Using different enzymes which are chemical scissors, they dismantled these missiles, examined their constituents and then prepared diagrams giving details of their internal assembly.
They found that every light chain consists of two parts of roughly equal lengths. In one half, the sequence of amino acids is constant while in the others it is variable. Again, in the variable region there are a few positions which are relatively free from variation.
This situation can be best illustrated by comparing the six words,

DEDICATION
REGULATION
DEPILATION
REPUTATION
SEPARATION
CORONATION

Even a cursory look at the letters in these words is sufficient to notice that it is made up of two parts of equal length. The latter half of these words has the same unchanged sequence of letters. Even in the first half where there is a great deal of variation some positions like the second are relatively invariant.

This ingenious structural mechanism endows each antibody molecule with its uniqueness. Since the location of the guiding instructions, the site at which it binds to an antigen, lies in the variable region it can home in onto the enemy like a hawk. Moreover, the heavy chain too has its own variable region besides three constant regions. This generates a phenomenally large number of permutations and combinations. That is how a separate antibody missile, each uniquely suited to take care of a particular enemy, can be manufactured.

The B-cells launch these missiles in the blood stream wading through which they go in search of the enemy. On finding it they embrace it tightly in an Indian death lock from which there is no escape.
Rodney Porter (left) and Gerald Edelman (right) deciphered the secrets of antibody structure by breaking it with different enzymes.
Certain enemies are more devious. Having gained entry by somehow deceiving the border guards they force their way inside an unsuspecting cell. They then make it their home and hold the unwitting host to ransom. They deprive the helpless host of its supplies and even use its equipment to sustain themselves. Viruses behave in this way and prosper. Even the insurgent cancerous cells are not much different.

However, the host still manages to display on its rooftop, the cell surface, at least a part of the standard bearer of the infiltrator. That alerts the $T_H$-cells which see this part of the foreign flag alongside the host’s own flag. The guided missiles of antibodies are not much effective against such hidden adversaries. The body, therefore, sends out tank-borne professional commandos of $T_C$-cells on the trail of these enemy hideouts.

These troops of cytotoxic T-cells kill the enemy by crashing on to their
The precise address is given to them by the T\textsubscript{H} cells which have detected the presence of these hidden enemies. Carrying that information T\textsubscript{C} brigades go on hunting for the hideouts that sport on the rooftops both their own flags and that of the lurking terrorist.

The reason that the host cells display their own identity card alongside that of the interloper is to ensure that the trigger happy T\textsubscript{C}-cells destroy only those that reluctantly harbour an enemy. Thus, T\textsubscript{C}-cells are also not diverted from their path by free intruder viruses which can be taken care of by the antibodies. The only regrettable part of this type of skirmish is that the host cell has to become a martyr in the process.

Both the B-cell armament factories and the tank brigade of T\textsubscript{C}-cells are pressed into activity by the T\textsubscript{H}-cells. The suppressor T-cells, T\textsubscript{S}-cells, on the other hand, keep a strict vigil both on B- and T\textsubscript{C}-cells lest they should get overenthusiastic and go berserk. The importance of T\textsubscript{H}-cells explains why AIDS is so deadly and why it results both in cancers and infections. The HIV responsible for AIDS, selectively attacks the T\textsubscript{H}-cells. Unaware of these developments, T\textsubscript{S}-cells diligently carry out their assigned task. The defence set-up thus is disastrously compromised.
There are times when the body puts into action yet another line of defence, that of using certain chemical weapons. When T\textsubscript{H} cells recognize the identity cards on the surface of cancerous cells or cells attacked by parasites they release these chemical weapons called lymphokines. These chemicals beckon macrophages to the site of the encounter and also incite them. The resultant angry macrophages can engulf and digest the beleagured cells.

The angry macrophages are not discriminating like the T\textsubscript{C} cells. They are not specific to an antigen. But since their action is local they attack only those cells that are recognized by the T\textsubscript{H} cells.

Interferon is another type of a chemical weapon. It inhibits the protein-making machinery of virus-infected cells so that the virus cannot proliferate. Further, it brings about changes in susceptible but uninfected cells conferring on them the ability to resist the virus.

The body thus has a variety of arrows in its quiver. It can adroitly select the one that is best suited to deal with the enemy.
Once an enemy, always an enemy. This may not be true in the world at large. The fickle nature and frailty of human beings make strange bedfellows. Today’s bitter foes may become bosom friends tomorrow. And vice versa. However, in the microcosmos of the body, the pathogenic enemies always retain their malafide intentions. If they are defeated once by the body’s defenders they may retreat, but only temporarily. They may lie low, only to raise their head at the first possible opportunity. They will continue to attack, again and again, whenever the conditions suit them.

The defence organization of the body, therefore, has acquired yet another special feature called immunological memory. This enables the lymphocytes to maintain recollection of the first encounter with an invader so that if it dares launch a fresh attack the cellular warriors can mobilize themselves swiftly and repulse the invasion with greater vigour.

On the first sighting of the enemy the border police cells as well as the $T_H$-cells take their own time making certain that the intruder is indeed inimical. Some more time elapses before they
pass on the signal to the command headquarters as well as themselves commence active collaboration with the armament manufacturing B-cells. The factories limber up a little lazily and need some more time to get themselves going at full throttle. The result is that for some time even after the first positive intimation of the enemy attack there is no appreciable retaliation.

Immunological memory persists throughout life After this dormant period the antibody missiles start making their presence felt, initially only in ones and twos. As much as a week or ten days may pass for the antibody missiles to gather strength and come charging down in full fury. It is only then that a battle royal ensues. This marks the beginning of the end of the misadventure engaged in by the enemy. The enemy certainly disappears fast. However, some T-cells carry with them a permanent imprint of the enemy's logo, his antigenic identification tag.

This memory stays for a long time, in some cases for the entire life span of the individual. If the enemy does not learn its lesson and has the temerity of invading again, the memory cells get the whole act together in no time. The alerted B-cells start a crash programme of assembling and launching the tailor-made antibody missiles which come pouring down on the enemy. The battle this time, called the secondary immune response, is much more fierce but lasts for a shorter time. The
memory cells carry out their job diligently irrespective of whether the missile dominated humoral response is to be launched or the tank battle of cellular response is to be joined.

The memory is highly specific too. It works only for that enemy which is returning to the hunting ground after having been driven away once. Those foes that invade the territory for the first time meet only a lethargic, somewhat delayed primary response giving them a temporary advantage.

This unique feature of immunological memory is the foundation of the practice of vaccination. Innoculation of a vaccine is like playing wargames to keep the troops in combat readiness. Vaccines introduce the lymphocytes to the antigenic passport of a potential enemy. This leads to establishment of immunological memory. When the real enemy invades it cannot take the defence forces by surprise because the immunological memory is now jolted. The alert forces immediately launch into a well prepared pitched battle. Victory follows in next to no time.

It was Edward JENNER (1749-1823) who devised these military exercises of vaccination some two hundred years ago. Neither he nor anyone else was aware then of the precise mechanism by which these wargames kept the cellular army on its toes though everyone had observed that people suffer from diseases like measles or mumps only once in their life. Jenner had heard milkmaids telling him that they were not afraid of the dreadful small pox disfiguring them because they had already suffered from the milder cow pox. Jenner
kept on making careful observations for a quarter of a century to verify this popular belief.

Once convinced he performed a most daring experiment on May 14, 1796. He staked his entire reputation, his very existence on this crucial experiment. He contacted one milkmaid, Sarah Nelms, who had got cow pox and sported several typical blisters on her arm. He took the contents from
one of these blisters and injected them into a healthy eight year old boy, James Phipps.

On the seventh day this brave lad experienced some pain in his armpit. Two days later he developed slight fever and complained of headache. But in a couple of days he recovered fully and was well. This, of course, was not unexpected since the effect of infection with cow pox was always mild.

Now Jenner embarked upon the very risky part of his experiment. On July the first, Jenner innoculated Phipps with human small pox taken directly from a festering pustule. Phipps remained free of the scourge of small pox. The practice of vaccination was born. What had happened was that the milder cow pox innoculation had given rise to a primary immune response. More importantly, it had generated immunological memory. When the small pox virus infected the boy it met with the vigorous and massive secondary immune response and was defeated speedily. The boy was saved from the ugly, dreadful manifestation of the disease.

It took a hundred years and another great scientist, the redoubtable Louis PASTEUR (1822-1895), for laying down the rules by which these war exercises of the body’s defence system can be staged. Pasteur had already demonstrated that diseases are caused not as a result of divine curse but because of infection by some disease carrying microorganisms. He had also shown the world quite convincingly that bacteria do not generate spontaneously but originate only from pre-existing organisms.

In 1880 he was studying chicken cholera. He had the culprit microbes growing in a test tube in his laboratory. Once, over a long weekend, the test tubes were inadvertently left at a higher temperature and with free access to air. Three weeks later when these bacteria were used to infect experimental birds the latter failed to contract the disease. When they were later infected with a fresh lot of bacteria the birds did not fall ill either.
Pasteur watches anxiously while his colleague gives Meister the first dose of anti-rabies vaccine.

He was reminded of what Jenner had observed in his experiments on smallpox. With ingenious reasoning he formulated the principles of vaccine preparation. He reasoned that if the enemy organisms were tamed and their face shown to the lymphocytes, the body's sentinels would quickly recognize the enemy's identity marks. The memory generated would enable them to deal with the real enemy if and when it attacked.

To prove his point Pasteur carried out two public experiments. In the first, conducted in May 1881, he injected 30
sheep and five cows on a farm at Pouilly-le-Fort with anthrax vaccine that he had developed. He kept an equal number of animals uninjected. On May 31, he infected all the 70 animals with live anthrax. All the animals that were not vaccinated fell prey to the affliction. But each of the 35 vaccinated animals remained healthy.

His second public experiment was even more dangerous. He had some rabbits that were infected with the rabies virus. When these animals were dead he separated their spinal cords and dried them in air. These were then ground to a fine powder from which he obtained a solution. This was his rabies vaccine with which he inoculated dogs which then became immune to the attack of hydrophobia.

He was convinced that the vaccine would prove equally effective for human beings. But nobody was prepared to go along with him. Then in 1895 people brought to him young Joseph Meister. The lad was bitten badly by a rabid dog which thus virtually signed his death warrant.

Pasteur decided to try a bold experiment. He injected Meister with the rabies vaccine. He repeated the injection a total of twelve times. That saved Joseph Meister’s life. He became the first human to survive after being bitten by a mad dog. Meister repaid his debt by becoming a watchman for the Pasteur Institute until his death.

Pasteur had thus shown that if the enemy forces are somehow made to
toe the path of non-violence, then such inactivated pathogens provide the dummy targets on which to train the body's warriors. Such debilitated organisms can generate a moderate primary immune response. But more importantly they elicit immunological memory and keep the body's sentinels on permanent but quiescent red alert with respect to that particular enemy.

Later it was found that if it is not easy to tame the enemy forces then their innocuous genetic cousins could also be used as dummy foes for the purpose of training the body's army. Jenner's small pox vaccine or the currently used oral polio vaccine developed by Sabin employ this very strategy.

In 1886, Salmon and Theobold-Smith quite accidentally found out that instead of using tamed enemy agents even enemy corpses could be used equally effectively for training purposes. Thus, another method for developing a vaccine was found. Salk's polio vaccine is of this kind. So are the typhoid, cholera and the whooping cough vaccines which consist of dead organisms.

Some other enemy organisms are crafty. They camp at one site but their destructive impact is felt at another. They are able to indulge in this guerilla tactic because they engage in chemical warfare. These organisms exude toxins which can spread through the body and damage cells at a distance. *Clostridium tetani*, the bacteria responsible for causing tetanus, for example, make their base in wounds on the surface of the body. But the poisonous substances they exude, cramp muscles some distance away. *Corynebacterium diphtheriae*, the bacteria that cause diphtheria, behave in a similar fashion. They grow in and around the tonsils forming a layer. The toxins that they exude, however, can affect the smooth functioning of the heart some distance away.

Here, a different strategy is employed against such long distance enemy. The body's defence organization is capable of retaliation even against chemical warfare. The enemy does
not necessarily have to be a living organism. It could even be a chemical. The sentinel cells can detect the identification marks of such a molecular 'enemy' and manufacture adequate antibody ammunition to inactivate and destroy that chemical.

A vaccine can, therefore, be prepared by processing the chemical in such a way that its poisonous sting is blunted without altering its antigenic characteristics. Introduction of such an altered toxin, toxoid in the immunologist's jargon, elicits a primary response and the life saving immunological memory. Vaccines against diphtheria or tetanus fall in this category.

The body's defence set up is, no doubt, highly impressive. And scientists keep trying hard to sharpen its cutting edge. But, in spite of these efforts, there are several enemies against which effective wargames cannot be staged. No useful vaccines are available as yet to combat the danger posed by malaria, jaundice, leprosy, infection by worms, the common cold and, in recent times, AIDS. The list can be even longer.

This does not mean that the body cannot or does not fight these attacks. But in the absence of crucial training imparted by a vaccine the body's defenders are somewhat handicapped. Their counter-offensive lacks punch.

There are many reasons for this apparent failure. In some cases the precise identity of the culprit organism has not yet been established. In others, the inimical organism employs a very clever manoeuvre. It keeps changing its antigenic cap frequently. It becomes difficult, therefore, to generate highly specific memory against this organism because the chemical identity tag keeps varying.

Certain organisms cannot be grown in the laboratory in adequate numbers. Therefore, efforts to tame them or to find milder genetic cousins cannot make much headway. Some like the HIV that inflicts the curse of AIDS, attack the very defence machinery. They selectively kill the T\(_H\)-cells.
Biotechnologists, however, are alive to this problem. They are constantly devising new methods to meet the challenge posed by these wily invaders. Consequently, trials are going on at present to test candidate vaccines that will help in dispelling the threat posed by malaria, leprosy, hepatitis - B.
a type of jaundice, even AIDS. In fact, scientists are even testing a vaccine to prevent pregnancy, thereby eradicating the social disease of overpopulation.
We have all heard of the story of the king's loyal guard who, in his over-enthusiasm, used a sword to kill the fly that was disturbing the sleeping king. The consequences of such a foolhardy venture can only be disastrous. The body's defence forces too get similarly overenthusiastic at times. The result is what is commonly known as allergy.

In 1905 the Austrian scientist Clemens Freiherr von Pirquet was studying the body's immune response to a protein he had extracted from the tiny bacteria that caused the devastating disease of tuberculosis (TB). When he injected this harmless protein in the skin of the forearm some patients, suspected to have TB, would develop over the next forty-eight hours a red, itchy, angry looking lump. This was called the tubercular reaction and was used as a test to confirm the clinical diagnosis.

To gain further knowledge of this phenomenon Von Pirquet conducted experiments using different proteins. Egg albumin was one such protein. He injected some guinea pigs with this in the hope that when a second injection was given in the skin of the foot
that the reaction occurred much faster, within minutes of the injection. Pirquet named this as “allergy”, to mean altered state of energy.

Initial curiosity about these quaint occurrences turned into an urgent concern when some of the subsequent experimenters observed that some animals developed the reaction so speedily and so violently that it resulted in painful death of the animal.

Much later, almost in the sixth decade of this century, it became clear that Pirquet’s understanding of the phenomenon and hence his nomenclature were not quite correct. The swellings or the rapid death occurred not because of an altered state of energy but rather due to an
overreaction on the part of the body's defence forces. It was an overenthusiastic response, too much of a good thing that turned sour. It has now been more aptly named, as hypersensitivity.

Allergic response is usually characterized by swelling, redness and itching

The mechanism by which this excessive response develops has also been discovered. On being alerted by the T_H-cells about an invasion by enemy microbes the B-cells start massive production of the antibody missiles. There are five different types of these missiles.

The antibody is made up of a globular protein. Since it plays such an important role in the immune response, this group of proteins is known as immunoglobulins. The five different classes are IgA, IgG, IgM, IgD and IgE.

Each one of these antibodies perform different functions. The one that is produced in very large numbers and whose use is also the maximum is the IgG. This missile bears the brunt of the body's battles. It can also cross the placenta, the protective covering of a child growing in its mother's womb. It thus protects the infant's body until it develops and hones its own defence organization.
The IgM antibody is a pentamer. Disulfide bond makes up the advance guard in the counter offensive operation. It is a massive molecule five times as big as the IgG. Bombardment with IgM in the early stages of the immune war softens the enemy and prepares the ground for the battle royal involving missile attack with the IgG. Whenever either of these missiles land on the enemy organism it activates a complex of proteins in the blood known as the complement. The complement acts as the chemical fuse for the warhead carried by the antibody missile. The resultant "explosion" kills the enemy. IgA is the preferred ammunition of the border security force. It is abundant in secretions like tears, saliva, mucus or breast milk.

The IgE, is the root cause of the "Emergency" created by hypersensitivities. IgE is, however, not manufactured solely for creating such
The heavy chains of the IgE antibody have an extra constant region.

emergencies. In fact, it has quite a useful role to play, especially in the early stages of the body's war against enemy pathogens.

For this purpose the body is equipped with a series of chemical mines. These are the mast cells which are liberally dispersed throughout the body. These cells carry a cargo of different sorts of chemicals. IgE acts as the trigger plunger of these mines. The mast cells have a specific receptor for the IgE by which the plunger gets hooked in its place. When this antibody reacts with the antigen the plunger gets pushed, the mine explodes and the chemical weapons inside are let loose.

Some of these chemicals such as histamine dilate the blood vessels in the areas under attack. This increases the flow of blood to that area. Naturally, the highly effective IgG missiles which are launched in the bloodstream also reach the area in strength and win the day for the body. The IgE are thus basically designed as an integral part of the ground battle plan.

Occasionally, however, the defence system goes overboard. And so the production of IgE is increased out of proportion. The large number of missiles, much more than needed, start attaching themselves to the chemical mines quite diligently. But since the proportion of these triggers to the mines is very high, each mast cell gets armed with too many triggers. Sometimes as many as 500,000 IgE molecules attach themselves to a single mast cell. Further such activated mines now extend all over the territory.
One can imagine what would happen in such an explosive situation. Even the slightest disturbance, the entry of even a small amount of the enemy antigen is enough to press the plungers and explode a large number of mines.

The resultant flood of chemicals dilate too many blood vessels. The sudden increased flow leads to angry swelling and hives. At the same time these chemicals have an opposite effect on the muscles which surround and control the airways. These muscles encompassing the windpipes that carry air in and out of the lungs start working spasmodically. Sometimes they compress the pipes restricting the flow of air. This results in wheezes, gasping for breath and asthma.

Unlike IgG, the IgE antibody preferentially gets attached to the surfaces of mast cells because it is different. It has a larger tail than the IgG. Its heavy chains have four regions of constant amino acid sequences instead of the usual three. It can thus get firmly embedded in the cell membrane.

This mutiny of the antibody bounty takes various forms. There are four different types of hypersensitivities, three that manifest slowly or in a delayed fashion. In addition there is an immediate type hypersensitivity that reveals its destructive potential within minutes. The Type I hypersensitivity is of the immediate kind that leads to an attack of asthma or rhinitis. Typical symptoms of allergic rhinitis are Watery nasal discharge, violent sneezing, runny eyes and itchy nose, throat and especially the roof of the mouth. Some patients suffer so badly that they sneeze as many as 50 times in rapid succession. Usually, the culprit allergen persists in the air surrounding the patient. It could be dust particles, skin flakes of some pet animals or molds.

There are two ways of curbing this mutiny. One constitutes a short term and immediate measure aimed at protecting the innocent cells from the ravages of this rebellion. Since the tissue damage is brought about through the action of chemical accomplices like histamine or leukotrienne, administra-
tion of antidotes that inactivate these chemicals provides relief.

This can, however, be only an interim and indirect measure. The armed chemical mines still lie waiting in anticipation of the entry of an allergen that will press the plunger. To provide a long term, and perhaps permanent, solution it is essential to generate the IgG type of antibodies which can latch on to the allergen before it can get attached to the cell bound IgE. Desensitization procedures leading to the manufacture of such blocking IgG missiles are now available. Of course, before embarking upon such a solution the culprit allergen has to be precisely identified.

The most dangerous manifestation of the Type I hypersensitivity is the violent extreme reaction called anaphylaxis. This can result in the death of an individual. Common allergens leading to an anaphylactic shock are some drugs like penicillin or insulin, insect stings, some fairly common food items like fish or eggs. Only immediate medical attention involving antidote injection can save the hapless person.

The Type II hypersensitivity results not from the IgE but the IgG antibody. Occasionally, the defence forces go crazy, lose their sense of propriety, mistake the identity tag on one of the body's own cells as an alien one and manufacture the IgG missile directed against that. When this missile lands on the target cell it can invite either the prowling killer cells or the blood borne complement system. This suicidal invitation results in the target cell's death.

Likewise IgE is not involved in the Type III hypersensitivity. The
Immune complexes are deposited in the tissue activating complement and attracting polymorphs. Immune complexes are formed as a result of the IgG missile latching on to the freely roaming intruder. Normally, such complexes are removed by the scavenger cells. If, however, there is an overabundance of them then the harried scavenger troops cannot cope with the workload. The uncleared complexes deposit themselves in the tissues, attracting the attention of patrolling polymorphonuclear leucocytes. The resulting interaction brings about some local damage.

There is yet another kind of hypersensitivity, the Type IV, classically known as the delayed type hypersensitivity (DTH). The rebel here is the T-cell which retains the memory of the intruder. On subsequent contact with the same enemy agent this cell releases chemical messengers in large bursts. This leads to inflammatory reactions. There is a further snowballing effect because the inflamed tissues attract macrophages which in turn flood the site with some more chemicals. Large red swellings, though limited to a specific location, is the result.

The body retains a strict and constant vigil that such mutinies of the bounty take place but rarely. However, since they are usually caused by the otherwise well meaning but overenthusiastic soldiers, they cannot be totally avoided.
No matter how well set a defence organization is, it is not always victorious. It does taste some crushing defeats at various times. The reasons are manifold. Sometimes the army is not well prepared. Rather there is a lack of training. Or the equipment is defective, even inadequate. At other times, the generals are incompetent. The intelligence network that has to provide vital information needed to work out a strategy fails to do its duty properly on some occasions. On other occasions, the enemy launches a massive offensive and the defending army is simply overwhelmed. Or else it unleashes a pre-emptive strike at vital installations throwing the command structure in disarray. The worst situation is when the enemy lies within making it difficult to distinguish between friend and foe.

The body's defence forces too encounter such tragic situations. In 1980, the extremely sad saga of an American boy David, then hardly six years old was brought to light by the mass media. The lad had been living in a world of his own. He did not, or rather could not, breathe the air around him. He had not experienced the
Poor David lived for twelve years in this sterile unit.

fragrance of flowers or the mouth-watering aroma of food. He had not known the warmth of a mother's embrace or the spontaneity of a friendly hug. Since his birth he had lived in a plastic bubble. Whenever he moved outside it was only after donning a specially made suit somewhat like the one worn by astronauts. He could only drink sterile water, breathe canned air and eat sterile food. Even the occasional toy he was allowed to handle had to be meticulously disinfected. David was living such an insipid life because he was born with a defective defence system that was ill equipped. It had a rabble of recruits that could not be trained. He was suffering from what is called primary immunodeficiency.

There are three types of such immunodeficiencies that exist from the birth and these are therefore termed congenital immunodeficiencies. In the first few weeks of their lives victims with such deficient defence organization remain healthy because the few antibody missiles that the mother installs in her offspring during pregnancy are still active. However, on expiry of the usefulness of this foreign aid, the opportunistic enemies which are always hovering around in the air, or on the skin or in the food get emboldened. Finding
A healthy person has both humoral and cellular defense systems functioning optimally.
In the absence of the cellular defense system, only a weak humoral attack can be launched. Absence or defect of the humoral system results in ineffective immune response.

Sometimes the defect lies in the recruiting centers themselves. The stem cells which are the precursors of the trained army of B- and T-cells are themselves defective or in short supply. This results in what is known as severe combined immunodeficiency. All forms of counter offensives, humoral as well as cellular, are seriously compromised. Enemies of all
kinds have a merry time at the expense of a defenceless victim.

Not all defeats are caused by shortage of trained soldiers; nor is a handicapped army the reason. There are situations when a fully functional, adequately manned immune army goes crazy. It loses its sense of propriety. It fails to distinguish friend from foe, self from non-self. As a result, it starts attacking the very territory it has to defend and this leads to autoimmune diseases.

A number of such afflictions have now been identified. Hashimoto’s thyroiditis which affects the functioning of the thyroid, Goodpasture’s syndrome that affects the kidneys, phacogeneic uveitis affecting the lens of the eye, haemolytic anemia causing lysis of red blood cells, myasthenia gravis which hampers the functioning of skeletal or even heart muscles and rheumatoid arthritis are a few examples of autoimmune disease. Some scientists think that even the more commonplace disorders like diabetes or leucoderma are also caused by autoimmune antibodies.

The exact reason why lymphocytes suddenly start producing antibodies against self antigens is not known. They are trained to tolerate and not to attack ‘self’ very early in life. Why they forget that is a mystery. Some scientists feel that as the body gets old its army too gets tired, even senile. It starts making more mistakes than usual. Others theorize that not all cellular antigens are expressed clearly during the embryonic stages. So, when the self antigenic flags are being demonstrated to the lymphocytic recruits during their early
Normally the humoral and cellular defense systems act only against NON-SELF. In autoimmune diseases they turn against SELF training these hidden flags remain out of sight. When they appear in the open in later life, the body's warriors quite naturally consider them to be alien and launch a vigorous attack. Whatever the reason, such autoimmune madness brings about large scale destruction.

If an autoimmune disorder is the result of a suicidal action of the cellular army, cancer is brought about due to its total inaction. Of course, the corporeal army cannot be blamed for this indifference because the unrest is caused by an internal insurgence. The primary function of any army is to provide protection from external threat. Only in exceptional circumstances is the responsibility to put down an internal rebellion given to it.

But the cellular army does not find this task to its taste. The major reason is that it is not easy to distinguish between the
terrorist rebel and the law-abiding citizen. They look so alike. Nor can the forces easily disobey their basic orders to tolerate self and go into war only against non-self. The army watches its own defeat helplessly.

Scientists have discovered in recent years that the cancer cells sport on their surface some specific antigens unique to them. These are known as tumour-specific transplantation antigens (TSTA). There is hope, therefore, that the body's army can be trained to recognize these as foreign and look upon the tumour as a foreign graft. The army's own inclination to drive out grafts can then be called upon to provide relief. Such attempts to use the immune system for cancer therapy are meeting with increasing success though the ultimate goal is still far away.

All these instances of defeat of the body's warriors are serious enough. But they pale into insignificance in comparison with that inflicted by the human immunodeficiency virus (HIV). This viral enemy specifically attacks the crucial battalion of T_H - cells. So the armament factories of B-cells cannot be given the orders to start production on a war-footing. Nor can the tank brigades of T_c-cells be alerted. Further, the T_s-cells, unaware of these developments keep carrying out their task faithfully.

When the resultant AIDS strikes, all those pathogenic enemy
microbes forever lurking around us seize the opportunity. Even the feeble ones come roaring in. The body is inundated with waves after waves of infectious attacks. Even the potential internal terrorists find courage. Cancers develop. With no defence of any kind whatsoever, permanent disintegration and total defeat can be the only result.
Not all the foreign visitors are undesirable. Not all enter with malafide intentions. Indeed some of them come to help, to assist indigenous growth efforts. Some are invited to participate in the developmental projects. Some provide vital raw materials or technology. The armed forces have to be restrained from attacking or stopping such esteemed guests.

Similar situation obtains in the body too. At times some crucial organ falters and does not carry out its assigned task to the optimum level. It may even stop functioning altogether. This, in turn, seriously affects the well being of the body. It can also pose the threat of death.

In the past, those hapless individuals whose kidneys or liver or heart had stopped functioning or one who had lost a large part of the skin faced certain death. Over the last three or four decades, however, relief is being provided by replacing the defective organ with a working one borrowed from someone else. The transplantation of an organ is being looked upon as an operation similar to transfusion of blood.
Howsoever beneficial such grafted organs are expected to be, the body's soldiers look upon them merely as of foreign origin. Since they operate on the principle of self and non-self, they consider anything foreign as harmful. Consequently, the body's defence forces launch an attack and the graft is rejected.

That such a rejection of a grafted organ is an immunological reaction was first observed by the British Nobel laureate Sir Peter MEDAWAR (1915-1987). During the second world war he was called upon to treat a large number of burn patients. One of their major problems was the severe loss of skin. Skin is one tissue that can grow. So Medawar started grafting pieces of skin on the bare parts of the body.
On a few occasions he was able to find sufficiently large areas of patient's body where the skin had not suffered any damage. He would, therefore, take pieces from these regions to transplant on bare patches. Such grafts readily took root and the patient's condition improved. More often, however, this was not possible as when the patient had suffered extensive burns. The skin for grafting had to be obtained from a donor. To his utter disappointment such grafts were always rejected. And if a second graft from the same donor was given it was rejected even faster.

This suggested to him that the body might be getting sensitized after the first graft which results in an immune response against the graft. He subsequently carried out a large number of experiments on animals and proved conclusively that the cells of the graft exhibited their own antigenic identities on their surface. These were read by the body's soldiers which then launched the cellular immune response leading to generation of killer T-cells.

![Graft rejection chart]

**Graft is rejected faster if the animal is previously sensitized**
Discovery of the cause for rejection was only half the work as far as Medawar was concerned. He was interested in saving his patients. Hence, he had to find ways of asking the body’s defence forces to declare a ceasefire.

Medawar, therefore, embarked upon experiments aimed at discovering the rules by which the body’s troops can be ordered to observe a selective ceasefire. This way, the grafted organs would not get rejected but the attacks of disease bearing organisms would still be repulsed.

He was helped in the design of his experiments by what an American scientist Ray OWEN had observed in 1945.

Twins, it is known, are of two different types. There are identical twins that originate from a single fertilized egg cell. In the scientific language they are called monozygotic twins. They have the same set of genes. Just as we cannot tell them apart the body’s sentinels too cannot see them as different from each other. Consequently they accept each other’s blood cells or skin or other organs as their own. No immune attack is launched.

On the other hand, there are non-identical or heterozygotic twins. These develop from two different egg cells that get fertilized at the same time. They are usually as
different from each other as are any other brother or sister. Consequently, the sentinels of one’s body recognize cells of the other as non-self and consider them as trespassers. The usual repulsive attack is launched against them.

Owen, however, observed that heterozygotic twin calves tolerated each other’s blood cells in their own stream. These apparently foreign blood cells were allowed to live happily without let or hindrance. This, he discovered, was due to the fact that when they were growing together in their mother’s womb their circulatory systems had come in very close contact. Therefore, blood from one had flown through the vessels of the other and vice versa. Later, in adult life, they were thus made to believe that the alien visitors are naturalized citizens.

Sir Frank MacFarlane Burnet, the father of modern immunology, in fact propounded a theory based on this observation. He stated that if during the period of embryonic development when the body is taking shape and its defence organization has not yet been established, the body encounters certain antigens, then later on it will not consider them as foreign. Those antigenic identity cards will be treated as being of self origin and tolerance will be shown towards their owners.

Medawar now set about to verify this hypothesis. A mouse normally spends 21 days inside its mother’s womb. So Medawar injected cells from the spleen and kidney of mice belonging to a different variety in such foetuses on the 15th day of gestation that is, six days before birth. When these mice became eight weeks old he grafted skins taken from those earlier donors. These were not rejected though the mice were capable of rejecting grafts donated by an altogether strange variety. The rules of immunological ceasefire had been discovered.

Of course, the knowledge of these rules is of little help when a human being is in need of a donation of an organ. It only tells the transplant surgeon to look for an identical twin.
Not everyone is, however, blessed with one. And the surgeon has to search for a suitable donor.

His task, however, has been made fairly easy by scientists like Jean DAUSSET (1916-), George SNELL (1903-) and Baruj BENACERRAF (1920-) who shared the 1980 Nobel Prize for Medicine. Once it became known that the rejection of a grafted organ or the body's expression of tolerance towards it are both immunological phenomena, scientists started searching for those identity
tags reading which the body's soldiers decide whether the visitor is self or non-self.

The situation is not much different from that of blood transfusion. The Nobel laureate Karl LANDSTEINER (1868-1943) had demonstrated the existence of the two major antigenic identity cards, A and B, on the surface of blood cells. These are read by the lymphocytes of the recipient to decide whether the transfused blood is compatible or not.

Dausset and other scientists following him showed that other human tissues also carry distinguishing antigenic markers on the surface of their cells. The body's defence forces read them to find out about their compatibility. These tell-tale antigenic flags are exhibited by the white blood cells also. That makes their identification in the laboratory as simple as determining the blood group. It is also because of this reason that these histocompatibility markers are called Human Leucocyte Antigens (HLA).

It also became known, mainly through the efforts of Snell and Benacerraf that the nature of these antigenic flags is decided by the genetic characteristics of the individual. Naturally, the HLA identity cards are acquired according to the laws of heredity. The complex of genes responsible for this is named as Major Histocompatibility Complex (MHC).

This complex plays a major role in defining the scope, nature and size of the command structure of the body's defence forces. It decides how strong the forces and their attack would be against an intruder. Since this part of the complex decides the strength of immune response to be launched against an antigen, it is known as the I-region or immune response region. Another product designed by genes in this complex acts as the identity card of the antigen presenting border security cells. When the T_h- cells read this MHC card along with that of the intruder they set in motion the retaliatory action of the body's defence forces.
The MHC gene defines the scope of the body's defense force

To surgeons interested in grafting foreign organs, finding out the HLA profile of an individual has become a very crucial step. Like the blood group analysis the HLA typing helps in choosing the suitable donor. For certain organs like kidneys, organ banks are now established with the HLA types neatly recorded. When a recipient is in need of a kidney his HLA type is communicated to these banks which then select the appropriate one.

In spite of this, however, exact matching of the donor graft to the recipient is not possible. There remains usually one or more of the several antigenic caps that the donated organ wears which are treated as foreign by the recipient's defense troops. Consequently an attack is launched against the visitor. However, it is not very strong. To quell this insurrection certain chemicals are used. These immunosuppressors
interfere in one of the chain of reactions that precede the formation and release of antibodies or the cytotoxic T-cells. Cortisone, prednisolone and 6-mercaptopurine are some of these immunosuppressors. Anti-lymphocyte serum (ALS) is also a powerful suppressor of immune response. Besides these, ionizing radiations can also hold the body's defenders in check.

However, none of these agents is selective in its action. They do not preferentially prevent the defenders from attacking the grafted benevolent visitor. They weaken the entire defence force, so that it is unable to protect the body from the opportunistic pathogenic enemies which always lurk around waiting for just such an opportunity. The ceasefire meant to be a selective one turns out to be of general nature and hence disastrous.

Other scientists, mainly Avrion MITCHISON of England, have found out means of making the defence forces observe selective ceasefire. They have shown that a single massive dose of an antigen induces immunological tolerance. The body fails to elicit an immune response to even a normal dose subsequently. This is called high zone tolerance.
On the other hand, repeated administration of small doses of the antigen also results in the same state of tolerance. This is referred to as low zone tolerance. This is one of the measures employed to overcome the mutiny of the bounty, the allergic condition.
Armies do not always engage themselves in war. Quite often they transform themselves into peacekeeping forces. They rub shoulders with civilians and provide help to those in distress due to natural calamity. They help in the reconstruction of buildings, roads and bridges. They also rush to the aid of another country threatened by an invasion.

The body’s armed forces do not on their own engage themselves into such activities. However, from time to time scientists try to enlist their help in providing succour to hapless individuals.

Emil VON BEHRING, (1854-1917) the German scientist who won the first ever Nobel Prize in Medicine in 1901 for his discovery of the antibody, made such an attempt on Christmas eve 1891. A year earlier, he had demonstrated the fighting potential of antibodies. On that historic day, he took sheep antibodies raised against diphtheria antigen and injected them into a little girl on the verge of death. Within hours the child started to recover.

Scientists at the time held high hopes for this type of treatment. But the useful life span of an-
Emil Von Behring drawing blood from sheep for passive immunotherapy
tibodies is small. They can, therefore, give relief only for a short time. Such **passive immunotherapy** can thus help only those who have suffered a temporary shortfall in their ability to produce potent antibodies. Moreover, to find a frequent donor of antibodies is not an easy task. Consequently, transfer of antibodies, or specific cells, as a therapeutic measure came to be slowly abandoned.

A revolutionary discovery in 1975 has, however, revived interest in using the powerful, highly specific guided missiles of antibodies not only for therapeutic but also for **diagnostic** purposes. Georges KOHLER (1946-) and Cesar MILSTEIN (1927-) succeeded in developing a **hybrid** cell that was immortal and also kept on producing large, almost unlimited quantities of potent, specific, and more importantly, identical antibodies. Development of this type of sturdy cellular factory, aptly named as **hybridoma**, has been such a momentous discovery that Kohler and Milstein were awarded the Nobel Prize for Medicine in 1984.
Any molecule of even a reasonable size has a number of configurations on its surface that are separately recognised by the body’s soldiers. Each of these which is a part of the antigenic flag of that molecule constitutes an **antigenic determinant**. A different antibody is manufactured to precisely take care of every single determinant. And each of these is produced by a different B-cell factory. It is expected that there pre-exist a million or more such independent B-cell factories.

Consequently, the total stockpile of these missiles manufactured in response to an antigen is a heterogeneous mixture. Although all of these missiles can ultimately account for the enemy, their homing abilities and fire powers vary. Moreover each factory has a limited span of productive life.

If the B-cell producing the most accurate and powerful antibody can be singled out and its life extended significantly, then it could be a great service to humanity. Kohler and Milstein did just that.

They were helped in their venture by nature which turns some B-cells into cancerous myeloma cells. These malignant tumours are immortal. Each tumour consists of a large number of totally identical cells, thus constituting a clone. Consequently, the phenomenally large numbers of immunoglobulin molecules it produces are all totally identical too.

Kohler and Milstein created a hybrid cell by fusing a myeloma cell with an antibody producing B-cell. Careful procedures of selection and refinement ascertained that the resultant hybridoma cell inherited the immortality of one parent and the ability to produce a useful antibody of the other. Such **monoclonal** antibody missiles which are programmed to home in on a single specific antigenic determinant target provide unprecedented help not only in therapeutic warfare but also in diagnostic intelligence gathering.
The protocol for the manufacture of monoclonal antibodies is simple:

1. **Induce and collect fluid containing antibodies**
2. **Fusion**
3. **Testing and Selection**
4. **Clone**
5. **Culture of myeloma cells**
6. **Spleen cells**
7. **Myeloma cells**

The availability of purified monoclonal antibodies in virtually unlimited quantities has opened up new vistas for the body's army. If, for example, precise monoclonal antibodies to TSTA can be obtained, they could perhaps be used to bombard the tumours. In a more practical way, however, scientists have thought of arming these missiles with the warhead of a powerful toxic drug. Since the missile would unerringly land only on the tumour cells, the toxic drug bomb would explode only in the insurgent cancer cell sparing the other law abiding cells. There is another ingenious idea taking shape. That is to encase the drugs in specially designed...
molecular containers called liposomes. These would be like trojan horses which will be guided by the antibody missiles to the exact address, on reaching which the drug-warriors hidden inside would at-tack the rebellious cancer cell.

The high degrees of purity and specificity of monoclonal antibodies have already made them effective intelligence agents. Analyzing these antibodies, scientists have learnt a great deal not only about their structural details but also
about the mechanism of their production. This, in turn, has enabled scientists to bring about further refinements in the machinery.

Since the monoclonal antibodies are highly specific, they are being used to identify antigenic determinants that are characteristic of certain cell types. For example, typing of the histocompatibility antigens, so crucial in transplantation of organs, has become much easier, thanks to the use of monoclonal antibodies. Needless to say they are being used even in blood typing.

Highly precise and accurate measurements of extremely small amounts of certain bodily secretions are essential for devising proper strategies for treating patients. For example, measurement of the hormones, T3 and T4, secreted by the thyroid provides valuable clues to the functioning of this gland. Doctors treating patients suffering from disorders of the thyroid can derive help from such measurements. They would then be able to tune their therapeutic regimens to greater level of efficacy. Techniques that permit such measurements, like radioimmunoassay or ELISA, rely on the property of specificity with which an antibody is endowed. Use of monoclonal antibodies has raised the accuracy and sensitivity standards of these techniques.

Isolation of a particular molecular species from a mixture and its further purification are also the arenas for peaceful uses of monoclonal antibody missiles. David SECHER and Derek BURKE in England prepared monoclonal antibodies against interferon. They attached those highly purified antibodies to an inert solid material and then used this column to obtain pure interferon from a heterogeneous mixture. Now such methods are being used even on an industrial scale.

Over the last few decades scientists have learnt a great deal about the working of this magnificent military of the human body. Nevertheless they are acutely aware that much more is still in the dark. And they are constantly trying to bring it
into light. As their knowledge of this fascinating defence network increases, they will be able to enhance its potential for preventing as well as winning the body's battles. Most of the time then it will not be necessary to wage wars. But when they become inevitable scientists will make sure that the wars will be shorter with more victories and very very few defeats.
**Glossary**

**Agammaglobulinemia:** A disorder which renders the body incapable of producing gammaglobulins or antibodies.

**AIDS:** Acquired Immuno Deficiency Syndrome. See HIV.

**Albumin:** A type of protein usually present in large concentrations in the fluid part of blood.

**Allergen:** Substances that cause allergies.

**Allergy:** A type of adverse reaction by the body’s immune system to a foreign substance. Though mostly mild, severe reactions may include shock and asthma.

**Amino acids:** Constituents of proteins. There are twenty different types.

**Anaphylaxis:** A severe type of allergic or hypersensitivity reaction that occurs speedily and can at times be fatal.

** Anthrax:** Also known as splenic fever and woolsorter’s disease, this acute infectious disease of sheep and cattle can also affect man. It is caused by *Bacillus anthracis*.

**Antibodies:** Type of proteins synthesized by the immune system in response to the introduction of an antigen. Antibodies are highly specific and bind strongly only to those antigens in response to which they are formed.

**Antigen:** Molecular configurations present on the surface of a substance that is like its own unique signature. Antibodies are formed against an antigen and are capable of binding to it.

**Antigenic determinant:** Part of antigen capable of acting independently.

**Anti-lymphocyte serum (ALS):** Fluid part of blood containing antibodies directed against antigens specific to lymphocytes of another species. ALS can suppress immune response in animals of the latter species.
**Autoimmune:** A reaction involving an immune response against the body's own tissues.

**Biotechnologist(s):** Scientist studying natural life processes with a view to controlling or manipulating them for specific mass applications.

**B-lymphocytes:** A subpopulation of lymphocytes that mature under the influence of the bone marrow.

**Bone marrow:** Porridge-like substance residing in the hollow of the bones.

**Bursa of Fabricius:** Lymph gland-like structure near the anus or cloaca in birds. Described for the first time by anatomist Fabricius in 1492.

**Candida:** (*C. albicans, C. tropicalis, C. parapsilosis and C. guilliermondii*). Species of yeasts present in healthy individuals that may become pathogenic or harmful under certain conditions such as malignancy or a defective immune system. Infection by *Candida* is called candidiasis or thrush.

**Carbohydrates:** A group of essential chemical compounds composed of carbon, hydrogen and oxygen. Carbohydrates provide energy and are present in foods rich in starch and sugar.

**Cellular immune response:** Type of immune response characterized by generation of cytotoxic T-cells.

**Cholera:** An acute infectious disease of the intestine caused by the comma bacillus, scientifically called *Vibrio cholerae*. Water contaminated with feces of infected people is the usual source of infection. Bacteria invade the body through the alimentary canal and symptoms like vomiting, violent abdominal cramps, severe diarrhoea characterized by pale rice water stools result. Disease may be fatal if treatment is delayed.

**Cilia:** Tiny hair-like structures lining the air tract.
Clone: Usually only genes are cloned to obtain a large number of identical copies. However, even single cells may be cloned.

Complement: A group of proteins present in the fluid part of blood. They are highly sensitive to heat.

Congenital: Present at birth but does not necessarily mean inherited.

Cytotoxic or killer T-cells (Tc): A subpopulation of T-lymphocytes capable of lysing target cells.

Diabetes: A condition where there is an abnormally high level of sugar in the blood.

Diagnosis: A systematic procedure used by doctors to detect the cause of a malady.

Diagnostic: Related to diagnosis.

Diphtheria: Acute infection of the throat and nose. The mucus membranes are attacked by bacterial toxins and the disease can be fatal if left untreated or if treatment is delayed.

Disulphide bridge: A chemical bond formed by joining of two sulphur atoms.

ELISA: Enzyme Linked Immuno Sorbant Assay. A method based on immunological properties permitting detection and measurement of minute quantities of body substances.

Enzyme: Protein molecule which acts as a catalyst in the chemical reactions in the body.

Fatty acids: Organic acids containing lipids or fats.

Foetus(es): Vertebrate embryo in egg or womb.

Fungi: Type of parasitic organisms that usually grow on dead or decaying materials.

Gammaglobulins: A type of globular protein present in the fluid part of the blood. Most of these possess the antibody activity.
Gene(s): The basic unit of heredity composed of molecules of deoxyribonucleic acid (DNA) and located on the chromosomes of each cell. Genes govern every single structural and functional characteristic of an individual.

Genetic: Pertaining to heredity.

Grafts: Transplantation of an organ.

Helper T-cells (TH): A subpopulation of T-lymphocytes engaged in recognition of foreign antigens and collaboration with B-lymphocytes for production of specific antibodies.

Hepatitis - B: A viral inflammation of the liver commonly known as jaundice. Formerly called serum hepatitis, this can spread via infected blood transfusion.

Heterozygotic: Developed from different fertilized egg cells. Homozygotic refers to those embryos developed from a single fertilized egg cell.

Histamine: A chemical naturally present in the body which dilates blood vessels.

Histocompatibility: Compatibility between two tissues (Histo=tissue).

HIV: Abbreviation used for the Human Immunodeficiency Virus which causes AIDS.

Hives: Urticaria or nettle rash. It is an allergic skin reaction characterized by itchy skin with reddish raised weals.

Human Leucocyte Antigens (HLA): Antigens that distinguish human cells from those of other species.

Humoral immune response: Type of immune response characterized by formation and circulation of antibodies.

Hybrid: Synthesis of two or more different characteristics; usually the offspring of genetically dissimilar parents.

Hybridoma: Hybrid cells formed by the union of antibody producing lymphocytes and myeloma cells.

Hydrophobia: See Rabies.
Hypersensitivity: Type of immune response which has an adverse impact. Also known as allergy.

Immune response: Physiological reactions to infections by disease causing organisms.

Immune system: Network of organs responsible for generating immune response.

Immunodeficiency: Anatomical or physiological disorder resulting in inefficient, subnormal or absence of immune response.

Immunoglobulins: Globular protein molecules synthesized during immune response. See gammaglobulins.

Immunosuppressors: Agents that suppress the immune response.

Infection: Invasion of the body by disease causing organism, with or without disease manifestation.

Insulin: Hormone made in the pancreas to maintain the level of sugar in the blood.

Interferon: A chemical secreted by the body to combat viral infection.

Ionizing radiations: High energy emissions that can split neutral atoms of matter into charged ions.

I-region: Part of the major histocompatibility complex of genes responsible for deciding the immunological potential of an individual.

Jaundice: Infectious disease caused by viral attack on liver cells resulting in accumulation of bile salts and pigments.

Lactic acid: Organic acid formed as a product of breaking down of glucose.

Leprosy: Infectious disease caused by Mycobacterium leprae.

Leucocytes: White blood cells.

Leucoderma: A disorder also known as vitiligo, where areas of skin lose their pigment and show up as pale patches.
Leukotrienne: A family of oxidized metabolic products of fatty acids. These are produced in certain cells upon stimulation and mediate responses in allergic reactions and inflammations of tissue.

Liposomes: Liposomes are vesicles where lipids enclose an aqueous space. These were first described by Alec D. Bangham and are thus also called Bangosomes. These are used in immunodiagnosis and in genetic engineering.

Lymph nodes: Glands housing lymphocytes.

Lymphocytes: Type of white blood cells that are responsible for affording protection against diseases.

Lymphokines: Chemicals that activate lymphoid cells.

Lysis: Breakdown of cells.

Lysozyme: Digestive enzymes contained in subcellular organelles called lysosomes. These can cause lysis of the cells.

Macrophages: Type of leucocytes capable of engulfing other cells. Engaged in scavenging tasks in the body.

Major Histocompatibility Complex (MHC): Part of the genetic legacy that generates proteins which characterize the uniqueness of tissues of a species.

Malaria: A disease caused by the blood parasite Plasmodium transmitted to humans by the bite of female Anopheles mosquitoes. Recurrent fever accompanied by shivering and chills is a common symptom.

Malignant: Abnormally altered cells capable of invading other organs. Usually associated with cancer.

Mast cells: A connective tissue cell which has large granules in the cytoplasm. These cells play an active role in allergies.

Mesenteric (lymph nodes): Lymph glands surrounding the intestines.

MHC protein: Type of protein formed according to the genetic blue print residing in that part of the genome known as Major Histocompatibility Complex.
Monoclonal: Derived from a single clone of cells.
Monozygotic: Embryos derived from a single fertilized egg. Such twins are genetically identical and therefore of the same sex.
Mucus: A clear, sticky lubricant secreted by glands in the mucus membranes that line the body cavity. It is normally produced in small amounts but infections can cause a dramatic increase in volume.
Myeloid (stem cell): The common progenitor cell from which the phagocytic or scavenger cells, for example monocytes and polymorphonuclear granulocytes, develop.
Myeloma: Cancerous development of B-lymphocytes.
Natural killer cells (NK): Type of leucocytes that preferentially inactivate virus-infected or cancerous cells.
Paratracheal (lymph nodes): Lymph glands surrounding the wind pipe.
Passive immunotherapy: Administration of antibodies from outside.
Pathogenic bacteria: Disease causing bacteria.
Penicillin: An antibiotic used against bacterial infections; derived from the mold Penicillium notatum. Discovered in 1928 by Sir Alexander Fleming.
Peyer's Patches: White, roundish patches of lymphatic nodules scattered along the inner lining of the intestinal walls; named after Johann Conrad Peyer, a Swedish anatomist.
Placenta: Organ, consisting of embryonic and maternal tissues in close union, by which the growing embryo is nourished in the womb. It also provides a protective cover for the growing embryo.
Pluripotent stem cell: Precursor cell that gives rise to different types of blood cells.
Polio: Short for poliomyelitis. A highly infectious disease caused by virus. The disease affects the central nervous system and can lead to impaired breathing, muscle wasting, paralysis and permanent deformity.

Polymorphonuclear granulocytes: Type of white blood cells.

Primary (immune) response: Immune response after the first encounter with an antigen.

Progenitor: Any living cell or organism that gives rise to progeny or offspring.

Protein: Building blocks of life.

Pyogenic: Giving rise to pus formation. This term is usually applied to bacteria.

Rabies: An acute almost invariably fatal viral infection of the brain. The virus is carried by rabid animals and human beings are infected by bites of these animals.

Radioimmunoassay: A method based on immunochemical properties and involving use of radioactively labeled molecules for measurement of very small quantities of body substances.

Rosettes: Composite of a lymphocyte surrounded by a number of red blood cells giving the appearance of a rose bud.

Secondary immune response: Immune response after second and subsequent encounter with an antigen.

Sensitized: An animal whose defence system is activated and is ready to launch a substantial immune response if challenged.

Spinal cord(s): The entire central nervous system except the brain, running through the vertebral column.

Spleen: A ductless organ, richly supplied by blood vessels lying adjacent to the stomach. It is an integral part of the lymphatic system, the basis of the body's defense against
infection. It is also concerned with the control of blood volume.

**Suppressor T-cells (Ts):** A subpopulation of T-lymphocytes that suppresses immune response.

**Syndrome:** A group of symptoms characterizing a disease.

**T3:** See Triiodothyronine.

**T4:** See Tetraiodothyronine.

**Tetanus:** Also known as lockjaw is caused by the bacteria *Clostridium tetani* which is found freely in manured soil and is common in animal dung. Tetanus is caused by a toxin that acts directly on the nervous system and produces spasms, generalized rigidity of the muscles and may lead to arching of the back and neck. The disease may be fatal due to disorders of control of vital functions such as heartbeat and blood pressure.

**Tetraiodothyronine:** One of the hormones secreted by the thyroid. It contains four iodine atoms and is called T4. Most of the hormones released from the gland are in this form.

**Third population of lymphocytes:** A subpopulation of lymphocytes different from B-, T-lymphocytes.

**Thymus:** Bilobed organ sitting astride the heart.

**Thyroid:** An endocrine gland found in the neck just below the level of the Adam’s apple (or larynx, the voice box). The gland has two lobes and makes the hormone thyroxine that governs tissue metabolism and growth.

**T-lymphocytes:** A subpopulation of lymphocytes that matures under the influence of thymus.

**Tolerance:** Condition characterized by inability to mount immune response.

**Tonsils:** A ring of lymphoid tissue which encircles the entrance to the food and air passages in the throat. They play a significant role in the immune system as their location is
ideally suited to scrutinize ingested material and to react to
those that pose a threat to the body.

**Toxic**: Poisonous.

**Toxoid**: A toxin that has been specially treated to destroy its
toxicity but still leaving it capable of inducing formation of
antibodies, for example tetanus toxoid.

**Transplantation**: Grafting of an organ from one site to
another.

**Triiodothyronine**: Another hormone secreted by the
thyroid. It contains three iodine atoms and is known as T3.
It is the active form of the hormone.

**TSTA**: Tumour Specific Transplantation Antigen. Antigens
present specifically on tumour cells but not on the analogous
normal cells.

**Tuberculosis**: Also called T.B., phthisis and consumption,
this is caused by the tubercle bacteria, *Mycobacterium tuber-
culos*is. Can affect any organ of the body though commonly
it attacks the lungs. This infectious disease attacks mostly the
weak and undernourished living under unhygienic condi-
tions.

**Tumour**: A mass of tissue that serves no purpose, arising as
a result of abnormal and uncontrolled proliferation of cells.
They are usually classified as benign (harmless) or malignant.
Malignant tumours usually grow faster than benign tumours
and invade other tissues thus creating a life-threatening
situation.

**Typhoid**: An infectious disease also known as enteric fever,
caused by the bacteria *Salmonella typhi*. Sources of infection
are contaminated water and food as also people who carry
the bacteria without showing any outward symptom of the
disease. Such carriers spread the infection when they handle
food. Deadly typhoid epidemics have occurred all over the
world in the past. Symptoms of typhoid are chills, headache,
backache, fever and rounded rose coloured spots on ab-
domen and chest. Treatment with chloramphenicol and sanitary measures have reduced typhoid cases.

**Typing:** Process of determining the profile of blood or tissue antigens.

**Vaccination:** Process to confer immunity against a disease.

**Vaccine:** Biological or chemical agent employed to evoke immunological memory against a disease.

**Virus:** Essentially a capsule of protein that contains either DNA or RNA as genetic material. There is debate as to if it is a living organism or a chemical entity. However, it has powers of reproducing when it invades a living cell.

**Whooping cough:** A contagious disease of the air passages caused by the bacteria *Bordetella pertussis* that causes inflammation in or near the wind pipe. The disease gets its name from the violent coughing attacks, each of which ends in a loud harsh 'whoop' when the breathless patient inhales through the mouth. Children aged between six months to eight years are especially at risk. There is no specific remedy but vaccine provides protection for six to 30 months.
"WAR makes rattling good history", said Oscar Wilde referring to the struggles of nations to capture new and to retain old territories. But other battles not visible to the naked eye are equally fascinating. An account of the miniscule wars fought within the confines of the human body is breathtaking if only for the fact that these are being fought every single living moment. The human body is continually besieged and attacked by a multitude of microbial enemies of great cunning and guile. However, nature has endowed the human body with an unique built-in defence organization that can be envy of the most modern technologically advanced nation.

This attractive and lavishly illustrated book, written especially for the non-specialist, unfolds the dramatic story of this inner defence organization, the diversity and specificity of its armament, and the methodical way in which it maintains a round-theclock vigil to meet squarely every imaginable threat to the human body and also how it wins the body’s battles most of the time.

About the Author.

Joint winner of the NCSTC National Award for the best S&T coverage in mass media, Bal Phondke is a prolific popular science writer not only in English but also in Marathi and Hindi. That he has a literary bent of mind is reflected in his science fiction.

After obtaining his M.Sc. (Bombay) and Ph.D (Lond.) in Nuclear Physics and Biophysics-Immunology respectively, Dr. Phondke served a 23-year stint as a research scientist in BARC during which he published about 100 research papers. From research he switched over to science communication and was the Editor of Science Today and Science Editor of the Times of India group of newspapers. He is currently the Director of Publications & Information Directorate (CSIR).